REMARKS

Claims 23 and 29 have been amended to refer to an amino acid region selected from the group consisting of His-Glu-Cys-Gly-His, His-Asp-Cys-Gly-His, or His-Asp-Cys-Ala-His, and to refer to the sequence identifier for each region. Support for the claim amendments can be found, for example, at page 29, Table 2. The specification also has been amended to incorporate sequence identifiers throughout the text. No new matter has been added. Applicants respectfully request reconsideration and allowance of claims 23, 25, 29, 37, 39-44, and 49-58 in view of the above amendments and following remarks.

Objection to the Specification

The Examiner requested that a new title be filed that reflects that the invention is directed to a method of increasing oleic acid content in seeds of transgenic plants comprising a mutant delta-12 enzyme with reduced linoleic acid in seed oil. Applicants have amended the title to recite "Methods for increasing oleic acid content in seeds from transgenic plants containing a mutant delta 12 desaturase." The Examiner is requested to withdraw the objection to the specification.

Rejections under 35 U.S.C. §112, first paragraph

Written Description

The Examiner rejected claims 23, 25, 29, 37, 39-44, and 49-58 under 35 U.S.C. §112, first paragraph, for lack of written description. The Examiner asserted that "Applicant does describe any other mutant delta-12 fatty acid desaturase polynucleotides other than SEQ ID NO:3 and 4 encoding amino acids of SEQ ID NO:7 and 8." The Examiner further asserted that "Applicants fail to describe a representative number of polynucleotide sequences encoding a mutant delta-12 fatty acid desaturase protein comprising a conserved His-Asp/Glu-Cys-Gly/Ala-His amino acid sequence, wherein a Lys is substituted for a Asp/Glu falling within the scope of the claimed genus of polynucleotides to be used in the claimed method of increasing oleic acid content in a plant seed" and furthermore, that "there is insufficient relevant identifying

characteristics to allow one skilled in the art to completely determine the structure of" such a polynucleotide. Applicants respectfully disagree.

An objective standard for determining compliance with the written description requirement is that the description must "clearly allow persons of skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ.2d 1614, 1618 (Fed. Cir.1989). Thus, the knowledge and level of skill in the particular art is a factor to be considered in determining compliance with the written description requirement. However, "the disclosure does not have to provide *in haec verba* support" for the claimed subject matter. Purdue Pharma L.P. v. Faulding Inc., 230 F.3d 1320, 56 USPQ2d 1481 (Fed. Cir. 2000).

The specification provides sufficient written description for claims 23, 25, 29, 37, 39-44, and 49-58, which recite that a Lys residue is substituted for Asp or Glu in an amino acid region selected from the group consisting of His-Glu-Cys-Gly-His, His-Asp-Cys-Gly-His, or His-Asp-Cys-Ala-His. Contrary to the Examiner's assertion, the specification describes more than the mutant delta-12 fatty acid desaturase polynucleotide and polypeptide of SEQ ID NOS: 3 and 4, respectively. For example, the specification lists wild-type delta-12 fatty acid desaturase nucleic acids from four different plant species (*Brassica napus*, *Arabidopsis thaliana*, *Glycine max*, and *Zea mays*); each of the polypeptides encoded by these nucleic acids contains one of the wild-type amino acid motifs recited in present claim 23. See, page 16, lines 15-22, and page 17, Table 1, of the specification. Since each of these nucleic acids contains a wild-type amino acid motif recited in present claim 23, one of ordinary skill would have immediately perceived that the inventors realized that a Lys residue could have been substituted for Glu or Asp in any of the recited motifs. See, e.g., specification at page 17, Table 1; page 28, lines 7-12; page 29, Table 2; and page 56, lines 24-26. As the Examiner knows, description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species the genus embraces. "If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention . . . even if [not] every nuance of the claims is explicitly described in the specification, then the adequate written description requirement is met." See Manual Patent Exam. Proc. §2163 II A 3(a) (citations

omitted). Here, one of ordinary skill would have realized that the inventors provided a representative number of species within the genus of polynucleotide sequences encoding mutant delta-12 fatty acid desaturases.

Second, the specification provides relevant identifying characteristics of mutant delta-12 fatty acid desaturases as recited in the pending claims, i.e., desaturases mutated in an amino acid motif having the sequence (in one letter amino acid code): HECGH, HDCGH, or HDCAH. These motifs are literally listed in the specification at, e.g., page 17, Table 1, row 3 and page 29, Table 2, rows 1, 2, and 3. Since the sequence of wild-type desaturases is provided in the specification, one skilled in the art could determine the structure of polynucleotide sequences encoding mutant delta-12 fatty acid desaturases, where a Lys is substituted for Asp or Glu in the recited motifs.

Finally, the Examiner referred to the polynucleotide and polypeptide of SEQ ID NOS: 7 and 8, respectively, as failing to provide support for the pending claims. Office Action, October 6, 2004 at page 3. Contrary to the Examiner's assertion, one of ordinary skill in the art would have recognized, based upon specification and the disclosed sequences of SEQ ID NOS: 7 and 8, that the inventors clearly had invented what is now claimed in claims 23, 25, 29, 37, 39-44, and 49-58.

The specification at page 39, lines 9-20, discloses that the mutant Q508 F delta-12 desaturase gene product (SEQ ID NO: 8), which is encoded by the nucleotide sequence of SEQ ID NO:7, does not inhibit endogenous wild-type delta-12 desaturase gene product. In other words, the mutant Q508F delta-12 desaturase gene product does not exhibit a dominant negative phenotype. Furthermore, the polypeptide whose amino acid sequence is set forth in SEQ ID NO: 8 does not carry a mutation as recited in the pending claims. One of ordinary skill in the art would have clearly understood from the dominant negative phenotype observed using SEQ ID NO: 4 and the lack of a dominant negative phenotype observed using SEQ ID NO: 8, that the inventors recognized that dominant negative suppression occurs when a Lys residue is substituted for Asp or Glu in a His-Glu-Cys-Gly-His, His-Asp-Cys-Gly-His, or His-Asp-Cys-Ala-His motif. See, e.g., specification at page 17, Table 1; page 28, lines 7-12; page 29, Table 2;

and page 56, lines 24-26. That is, the lack of a dominant negative phenotype with sequences that do not have the claimed mutations would have clearly confirmed to one of ordinary skill that the inventors invented the subject matter of claims 23, 25, 29, 37, 39-44, and 49-58.

Accordingly, one having ordinary skill in the art would have recognized that there is more than adequate written description for coding sequences encoding delta-12 desaturases having a Lys residue substituted for Asp/Glu in a His-Glu-Cys-Gly-His, His-Asp-Cys-Gly-His, or His-Asp-Cys-Ala-His motif. The Examiner is requested to withdraw the rejection of claims 23, 25, 29, 37, 39-44, and 49-58 under 35 U.S.C. §112, first paragraph, for lack of written description.

Enablement

The Examiner rejected claims 23, 25, 29, 37, 39-44, and 49-58 under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner asserted that "Applicant does not teach a method of increasing levels of seed oleic and lowering linoleic and linolenic acid resulting in ranges of above 78.6% for oleic acid (18:1), and lower than 6.4% for linoleic acid (18:2), and lower than 4.51% for linolenic acid (18:3). The Examiner asserted that increasing oleic acid content and decreasing linoleic and linolenic acid content in the seeds of plants using a mutant form of the endogenous delta-12 desaturase is unpredictable as "this type of mutational inhibition or dominant negative inhibition of gene expression is leaky and requires multiple gene expression strategies to achieve levels of oleic acid in plant seeds such that seed oleic acid levels increase to 90% and linoleic and linolenic acid levels decrease to 1%." and cited Lightner et al., U.S. Patent No. 6,372,965 (column 65, Table 18 and column 66, Table 19 and lines 22-27) and Osawa et al., J. Biol. Chem., 1991, 266(8):4673-4676. Applicants respectfully disagree with the Examiner because the specification enables one of ordinary skill in the art to practice the methods of claims 23, 25, 37, 39-44, and 49-58 and make and use the recombinant nucleic acid construct of claim 29.

The inquiry with respect to scope of enablement under 35 U.S.C. §112, first paragraph, is whether it would require undue experimentation to make and use the claimed invention. A

considerable amount of experimentation is permissible, particularly if it is routine experimentation. The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'f 1986); see also In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). A consideration of these factors with respect to the present application demonstrates that, in conjunction with what was known to one of skill in the art, the specification teaches how to make and use the full scope of the claimed subject matter.

First, the oleic acid, linoleic acid, and linolenic acid percentages that the Examiner refers to for the present application are from T2 seeds. T2 generation plants are not homozygous for the introduced gene. See, for example, specification at page 39, line 1. The specification teaches that T3 and subsequent generations, which are homozygous for the mutant delta-12 desaturase gene, will have lower levels of linoleic acid and linolenic acid and higher levels of oleic acid, relative to the T2 generation. See, for example, specification at page 39, lines 2-8.

Second, an oleic acid content of >85% was achieved by Lightner et al. in plants containing a single transgene (i.e., an antisense microsomal delta-12 desaturase construct). See, for example, Tables 15 and 16 of Lightner et al. In view of the teachings in the specification and in Lightner et al., one of ordinary skill would have been aware that "multiple gene expression strategies" were not necessary, and that no more than routine experimentation would have been required to make seed oils having greater than 78.6% oleic acid, lower than 6.4% linoleic acid, and lower than 4.51% linolenic acid.

Third, the Examiner has misapprehended the scope of the claims and the teachings of the specification. The specification at page 39, lines 9-20, discloses that the mutant Q508 F form delta-12 desaturase polypeptide (SEQ ID NO: 8) does not inhibit endogenous wild-type delta-12 desaturase gene product, i.e., does not exhibit a dominant negative phenotype. The polynucleotide of SEQ ID NO:7, which encodes the polypeptide of SEQ ID NO:8, does not carry a mutation as recited in the pending claims. Rather than demonstrating unpredictability, the

teachings in the specification concerning the polynucleotide and polypeptide of SEQ ID NOS: 7 and 8, respectively, would have confirmed to one of ordinary skill in the art that delta-12 fatty acid desaturases carrying the claimed mutations would alter fatty acid composition in a different manner from desaturases, such as SEQ ID NO: 8, carrying mutations elsewhere.

The Examiner also asserted that the claimed range for linolenic acid was stated to fall both above and below wild-type levels for the variety Westar reported in the Lightner et al. patent. Office Action October 6, 2004 at page 7. Applicants respectfully disagree.

First, the Examiner has referred to only one Table in the Lightner et al. patent. Lightner et al. also report in Table 19, column 66, that the linolenic acid levels for Westar are 10.60%. Thus, upon reading the entire Lightner et al. specification, one of ordinary skill would have realized that linolenic acid levels of from 1 to 10% could have been readily attained. Second, there are a number of other plant varieties known in the art in addition to the Westar variety, some of which have linolenic acid levels that are much higher than Westar. See, e.g., page 68, Table 3 of Rakow, Z. Pflanzenzüchtg, 69:62-82 (1973). A copy of the Rakow article is attached in an Information Disclosure Statement submitted herewith. Thus, one of ordinary skill would have been able to make and use the invention as claimed in claims 25, 43 and 44, by using a variety other than Westar.

The Examiner also asserted that the "state of the art for a method of increasing oleic acid content in seeds using a mutant or dominant negative protein comprising mutated conserved regions to eliminate gene expression is unpredictable because the resulting modified proteins can be either leaky resulting in an incomplete inhibition of gene expression, or produce mutant proteins that have the opposite effect" and cited page 4674 of Osawa et al. The Examiner further asserted that "unknown regulatory or structural properties of a homologous protein can have unexpected results when attempting to engineering [sic] analogous activities into related proteins by transposing peptide modifications." Applicants respectfully disagree.

First, the Osawa et al. article supports the Applicants' position rather than the Examiner's position. Osawa et al. conclude on page 4676 that a particular motif is conserved in all G protein α chains to date and that "similar mutations to $Gly^{225} \rightarrow$ Thr should generate dominant negative

mutants in other G protein α chains." Thus, rather than supporting a conclusion that the claimed invention is unpredictable, the Osawa et al. reference supports a conclusion that the claimed invention is highly predictable. Second, as discussed above, the specification lists four wild-type delta-12 fatty acid desaturase nucleic acids from the plant species *Brassica napus*, *Arabidopsis thaliana*, *Glycine max*, and *Zea mays*; each of the polypeptides encoded by these nucleic acids contains a wild-type amino acid motif recited in present claim 23. See, page 16, lines 15-22, and page 17, Table 1, of the specification. Since each of these nucleic acids have a high degree of sequence similarity as disclosed in Lightner et al., and encode an exact amino acid motif to be mutated as recited in the present claims, the state of the art was sufficiently developed to permit one of ordinary skill to practice the invention.

The Examiner further asserted that "undue trial and error experimentation would be required for one of ordinary skill in the art to screen through a multitude of non-exemplified transformed plants comprising any one of a myriad of delta 12 desaturase proteins comprising a mutant delta-12 sequence having a Lys substituted for a Asp/Glu in a (Ala/Gly)-His-(Asp/Glu)-Cys-Gly-His conserved sequence to identify those polynucleotides that when transformed and expressed in plants produce plants having seeds with increased oleic acid levels as high as 90% and linoleic and linolenic acid levels as low as 1%."

Applicants disagree. As indicated in §2164.01 of the MPEP, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is undertaken, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). In the present case, analysis of the claimed plants is typical of that carried out in the art and experimentation is not complex. The specification provides the amino acid sequences of delta-12 desaturases and indicates that the recited motif is conserved among the known delta-12 desaturases. See specification at page 13, lines 23-30. The specification also provides the mutation to be introduced into such a motif (i.e., Lys for Asp/Glu) and indicates that sequence modifications are routine to one of skill in the art. See, e.g., page 12, lines 14-16 of the specification. The specification also provides detailed guidance for generating recombinant nucleic acid constructs and introducing such constructs into plants. See, e.g., page 18, line 28 through page 19, line 6,

page 20, line 33 through page 26, line 22 of the specification. Plants can be grown and selfed using the methods described, for example, on page 35, lines 8-19 of the specification. Fatty acid profiles of seeds can be determined using the methods described in WO 93/11345. See, specification page 35, lines 26-27. Thus, only routine experimentation would have been necessary to produce the claimed plants.

In view of the above remarks, the Examiner is requested to withdraw the rejection of claims 23, 25, 29, 37, 39-44, and 49-58 under 35 U.S.C. §112, first paragraph, for lack of enablement.

CONCLUSION

A petition for extension is being filed with this response along with the $1,020 fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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